



Reply to Office Action
Application No. 09/127,364
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R E M A R K S

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks.

Claims 1-10 are now in this application.

Amendments

The specification was amended at pages 1, the bridging paragraph on pages 13-14, and pages 18, 20, 32 and 35 to insert provide the relevant serial numbers for the variety of U.S. provisional, U.S. regular and PCT applications cited therein.

The specification was further amended at page 8, line 11, by inserting the definitions for the various substituents as found in U.S. Patent Application Serial No. 08/904,424 which application was incorporated by reference in its entirety. See, for example, page 1, lines 4-8, of the specification. Insertion of these definitions is necessary in order to provide metes and bounds for the recited groups in the compound of the formula $R^1-SO_2-NR^2-CHR^3-Q-CHR^5-CO_2H$ found in the specification and in Claims 7, 16 and 22.

In addition, obvious errors were corrected at page 18, line 15; page 20, line 19; page 32; line 5; and page 35, line 16.

Claims 11-23 were canceled without prejudice or disclaimer in view of the first restriction requirement issued for this application. Applicants reserve the right to file one or more divisional applications directed to the canceled subject matter.

No new matter has been added. Entry of these amendments is earnestly solicited.



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As required by 37 C.F.R. §1.121, these amendments are specified in the attached Appendix.

Second Restriction Requirement

In the Office Action, a second restriction requirement was set forth in which the claims in this application were grouped as follows:

- Group 10: Claims 1-6, 9 and 10 drawn to compounds disclosed in application 08/904,415;
- Group 11: Claim 1-6, 9 and 10 drawn to compounds disclosed in application 08/903,585;
- Group 12: Claim 1-6, 9 and 10 drawn to compounds disclosed in application 08/904,423;
- Group 13: Claim 1-6, 9 and 10 drawn to compounds disclosed in application 08/920,353;
- Group 14: Claim 1-6, 9 and 10 drawn to compounds disclosed in application 08/904,417;
- Group 15: Claim 1-6, 9 and 10 drawn to compounds disclosed in application 08/920,394;
- Group 16: Claim 1-6, 9 and 10 drawn to compounds disclosed in application 08/904,416.
- Group 17: Claim 1-6, 9 and 10 drawn to any compound that is encompassed by claim 1, with the proviso that subgenus G1 (as defined in the Office Action) is excluded, and with the further proviso that all compounds that are explicitly recited in application 09/127,364 are also excluded.

This second restriction requirement is traversed-in-part. Initially, Applicants do not traverse the eight groups identified above but, for the following reasons, submit that there should be a ninth grouping. Specifically, while this restriction requirement is grouped, in part, by the seven applications identified above, there is an eighth application, U.S. Serial No. 08/904,424, which should be included within this restriction requirement. The compounds of this last application are directed to carbamyloxy compounds as recited in originally presented Claims 7, 16 and 22 of the present application. Moreover, each of the compounds specifically recited in originally presented Claims 4, 8, 9-11, 14, 17 and 21 of this application recite carbamyloxy compounds. It is, in fact, these compounds which Applicants, if given the option, would elect.

Applicants further note that because the compounds of Claims 4, 9 and 10 of this application are carbamyloxy compounds, inclusion of Claims 4, 9 and 10 in Groups 10-16 is improper because these compounds simply do not correlate to the prior filed U.S. application which is relied upon to restrict these groups.

Based on the above, Applicants request that this restriction requirement be recast as follows:

- Group A: Claims 1-3, 5 and 6 drawn to compounds disclosed in U.S. Patent Application Serial No. 08/904,415;
- Group B: Claim 1-3, 5 and 6 drawn to compounds disclosed in U.S. Patent Application Serial No. 08/903,585;
- Group C: Claim 1-3, 5 and 6 drawn to compounds disclosed in U.S. Patent Application Serial No. 08/904,423;
- Group D: Claim 1-3, 5 and 6 drawn to compounds disclosed in U.S. Patent Application Serial No. 08/920,353;

Group E: Claim 1-3, 5 and 6 drawn to compounds disclosed in U.S. Patent Application Serial No. 08/904,417;

Group F: Claim 1-3, 5 and 6 drawn to compounds disclosed in U.S. Patent Application Serial No. 08/920,394;

Group G: Claim 1-3, 5 and 6 drawn to compounds disclosed in U.S. Patent Application Serial No. 08/904,416.

Group H: Claims 1-6, 9 and 10 drawn to compounds disclosed in U.S. Patent Application Serial No. 08/904,424

Group I: Claim 1-3, 5 and 6 drawn to any compound that is encompassed by claim 1, with the proviso that subgenus G1 is excluded, and with the further proviso that all compounds that are explicitly recited in application 09/127,364 are also excluded.

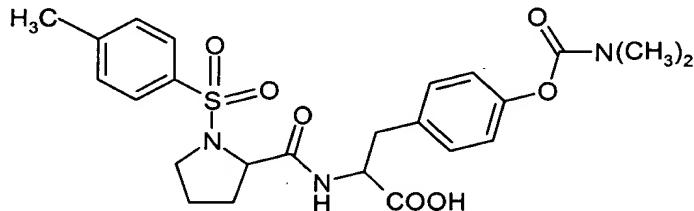
If so recast, Applicants would elect Group H.

Election

Notwithstanding the above traversal, Applicants are required to make an election consistent with the second restriction requirement found in the Office Action mailed on November 15, 2000. Accordingly, Applicants elect, with traverse (as noted above), Group 10.

Election of Species

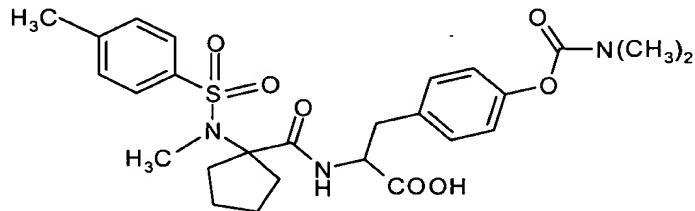
Applicants were further required to either confirm the previously elected species (if this species was consistent with the elected group) or to elect a new species. In this regard, Applicants previously elected as their species the compound:



Applicants note, however, that this compound is not within any of Groups 10-17 identified in the Office Action of November 15, 2000 but, rather, corresponds to Group H of the suggested recasted restriction requirement.

If recasted, Applicants will continue to elect this species consistent with their desired election of Group H.

To the extent that this restriction requirement is not recast, Applicants note that there are no species specifically disclosed in this application which correspond to elected Group 10. However, in order to prevent non-compliance with the election of species requirement, Applicants would elect the following compound found in U.S. Patent Application Serial No. 08/904,415:



This compound corresponds to the sixth compound found at page 26 of Serial No. 08/904,415. Claims 1, 2, 3, 5 and 6 of this application are believed to read on this species.



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Early examination on the merits is earnestly solicited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: Gerald F. Swiss
Gerald F. Swiss
Registration No. 30,113
Attorney for Applicants
Redwood Shores, CA Office
(650) 622-2300

P.O. Box 1404
Alexandria, Virginia 22313-1404

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Reply to Office Action
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Page 1

Attachment to Reply and Amendment dated March 15, 2001

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Amendments to page 1, lines 4-8:

This application claims the benefit of U.S. Provisional Application No. [60/____,____] 60/112,020, which was converted pursuant to 37 C.F.R. § 1.53(c)(2)(i) from U.S. Patent Application No. 08/904,424, filed July 31, 1997, and of U.S. Provisional Application No. 60/054,453, filed August 1, 1997, all of which applications are incorporated herein by reference in their entireties.

Amendments to the paragraph bridging pages 13 and 14:

Studies carried out in support of the present invention have revealed that compounds which modulate binding of alpha-4/beta-1 integrin to any of its ligands, including VCAM-1, are generally also good candidates for modulating binding of alpha-9 integrin to its ligand(s). More specifically, as described in section IV, below, specific antagonists of alpha-4/beta-1 integrin also block alpha-9 integrin binding to tenascin. This discovery therefore provides a wealth of candidate compounds for use in pharmaceutical compositions and methods of the present invention. For example, co-owned, concurrently-filed related application [USSN _____, (PCT _____)] U.S. Serial No. 09/126,958, (PCT Serial No. PCT/US98/15324) incorporated herein by reference, which claims priority to the same initial U.S. Patent Applications, U.S. Patent Application No. 08/904,424, filed July 31, 1997, and U.S. Provisional Application No. 60/054,453, filed August 1, 1997, which are incorporated herein by reference in their entireties, describes a series of carbamylxy compounds which have been characterized as inhibitors of alpha-4/beta-1 integrin binding to its ligands (*i.e.*, $\alpha_4\beta_1$ antagonists). Testing and use of several exemplary compounds of this series are discussed below. Methods for making such compounds are detailed in Example 4 herein.



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Amendments to the paragraph at page 18, lines 9-16:

Table 1 lists exemplary alpha-4/beta-1 integrin inhibitory compounds that were found to have activity in the foregoing assays. Moreover, experiments in support of the present invention revealed that all 373 compounds described in parent applications U.S. Patent Application No. 08/904,424, filed July 31, 1997, and U.S. Provisional Application No. 60/054,453, filed August 1, 1997, and/or in co-owned application [PCT/US98/____] PCT/US98/15324 filed concurrently herewith, all of which are incorporated herein by reference, exhibited sufficient [alpha-4-beta-1] alpha-4/beta-1 integrin inhibitory activity to be considered candidates for alpha-9 screening, as described in Part B, below.

Amendments to the paragraph at page 20, lines 14-20:

Methods for preparing the above-referenced reference standard compounds are found, for example in Example 4 herein (compounds 1-6), in parent application U.S. Patent Application No. 08/904,424, filed July 31, 1997, or U.S. Provisional Application No. 60/054,453, filed August 1, 1997 (both of which are concurrently filed with the present application as [PCT/US98/____] PCT/US98/15324 []), or in U.S. Patent Application No. 08/920,394, filed July 31, 1997, filed concurrently as [PCT/US98/____] PCT/US98/15313), all of which are incorporated herein by reference.

Please amend the paragraph at page 32, lines 4-6, to read as follows:



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When tested in this assay, each of the compounds as described in Examples 1-373 of parent application [USSN] U.S. Serial No. 08/904,424 [(PCT/US98/____)] (PCT/US98/15324) or the corresponding carboxylic acids of the ester compounds [,] (i.e., the prodrugs) exhibit IC₅₀s of 15 μ M or less.

Please amend the paragraph at page 35, lines 16-23, to read as follows:

This Example provides representative organic syntheses of [pre-cursors] precursors and reference standard compounds described herein. Parent applications U.S. Patent Application No. 08/904,424, filed July 31, 1997, and U.S. Provisional Application No. 60/054,453, filed August 1, 1997, as well as co-owned, concurrently filed US Patent Application No. [_____] 09/126,958 and corresponding PCT application PCT/US98/____] PCT/US98/15324 all of which applications are incorporated herein by reference in their entireties, are referenced specifically for their methods of preparation of these and many other related compounds.